

In re Application of:
Evan C. Unger
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REMARKS

A. The Status of the Claims and the Amendments

Claims 132-137, 142-145, 152-159, 161-163, 167, and 175-177 have been previously canceled without prejudice, as claims drawn to non-elected species. Claims 185-250 have been withdrawn as claims drawn to non-elected species.

By the present amendment, claims 116 and 164 have been amended to claim the invention with greater particularity and specificity. Specifically, some matter previously introduced and objected to by the Examiner as allegedly a "new matter" has been deleted. No new matter has been introduced in the amendments and in new claims 251-267. Accordingly, entry of the amendment is respectfully requested.

Upon entry of this amendment, claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, and 178-253 will be pending, of which claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, 178-184, and 251-267 will be under consideration.

B. Restriction Requirement

The Examiner has stated that claims 226-250 are directed to non-elected species and has withdrawn them from consideration (page 3 of the Office Action). The Applicant respectfully disagrees.

Previously, the Applicant pointed out that claims 226-250 combine the matter that was elected and that there was no logical reason for their being withdrawn (see the response filed May 23, 2006, responding to the final Office Action mailed February 24, 2006). Indeed, the Applicant explained that claims 226-250 represent combinations of the original claims 121, 123, 124, 126, and 128. The Applicant further pointed out that none of these original claims had been withdrawn from consideration as directed to a

non-elected invention and that each is currently under consideration. Finally, the Applicant respectfully reminds the Examiner that claims 226-250 were added in response to the suggestion made by the Examiner's during the interview on August 2, 2005.

However, the latest Office Action did not address any of these points and the Examiner continues to insist claims 226-250 are directed to non-elected matter, without explaining why the Applicant's argument to the contrary is invalid. It is also submitted that if an Examiner recommends adding some claims, it would not be proper to object to them once the Examiner's suggestion has been followed. In view of the foregoing, reconsideration and reinstatement of claims 226-250 are respectfully requested.

C. Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, 178, and 179 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention (the written description requirement) (page 4 of the Office Action). More specifically, the examiner has stated that the limitation "delivering said bioactive agent from the vasculature through the vessel wall and into said selected tissue" is not disclosed in the original specification, and thus constitutes new matter.

While the Applicant respectfully disagrees with such characterization and submits that the original specification contains the above-mentioned limitation, at least implicitly or inherently, in the interest of facilitating the process of prosecution of this application claims 116 and 164 have been amended and the words "from the vasculature through the vessel wall" have been deleted.

Accordingly, it is submitted that the rejection no longer applies. In view of the foregoing, reconsideration and withdrawal of the rejection of claims 116-131, 138-141,

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146-151, 160, 164-166, 168-174, 178, and 179 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

D. Rejections Under 35 U.S.C. § 103(a)

Claims 116-125, 129-131, 138-141, 146-151, 160, 164-166, 168-174, 178, and 179 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,695,460 to Siegel et al., in view of U.S. Patent No. 5,334,381 to Unger "Unger '381"), and further in view of U.S. Patent No. 5,648,098 to Porter (page 6 of the Office Action). This rejection is respectfully traversed.

The three basic criteria that must be met to establish a *prima facie* case of obviousness have been provided and discussed in responses to previous Office Actions. Applicant submits that the Examiner has not established a *prima facie* case of obviousness.

More specifically, each of claims 116 and 164 requires "applying to the patient ultrasonic energy having a frequency between about 750 kHz and 3 MHz."

Siegel et al. fail to describe or suggest a method which includes all the limitations recited in claims 116 and 164. Specifically, Siegel et al. only teach a method of thrombolysis in which preferably the frequency between 24 and 53 KHz is used (col. 2, lines 46-47), especially 25-39 KHz (col. 7, lines 59-60). Siegel et al. fail to describe or suggest any frequency that is higher than 243 KHz (col. 7, lines 46 and 57). Accordingly, there is nothing in Siegel et al. disclosing or suggesting the use of such high frequencies as 750 kHz to 3 MHz, required by the instant claims 16 and 64. Combining Siegel et al. with Unger '381 fail to cure this deficiency, and the Examiner has correctly recognized that such a combination does not teach use of a frequency between about 750 kHz and 3 MHz.

To cure these deficiencies of Siegel et al., the Examiner proposes to combine the teachings of Siegel et al., Unger '381 and Porter. The Examiner's proposal to combine Siegel et al., Unger '381 and Porter is based on the fact that Porter mentions a possibility of using the frequency up to several megahertz, which overlaps with the range of frequencies between about 750 kHz and 3 MHz recited in each of claims 116 and 164.

However, such combination of references still fails to set forth a proper prima facie case of obviousness, because there is no any suggestion or motivation to modify the Siegel et al. (i.e., Siegel's use of low frequencies) by importing the teachings of Porter to arrive to the high frequencies recited in the instant claims 116 and 164. The Examiner's conclusion of combinability of Siegel et al., Unger '381 and Porter is based upon Porter's mentioning a possibility of using frequencies in the range claimed in claims 116 and 164. The Applicant respectfully submits that such mentioning is not enough.

Indeed, the case law is clear that the desirability of modification proposed by an Examiner must be provided by the very references that are relied upon for making a prima facie case of obviousness. The Applicant previously stated that there is no such suggestion of desirability in any of the references. The Examiner has declined to accept this argument, and the Applicant submits that the approach taken by the Examiner is erroneous and respectfully requests reconsideration.

The only reason in favor of modification of Siegel et al. using Porter, as provided by the Examiner, is that such modification is merely "optimization" and that discovering the optimum range by routine experimentation "is not inventive," as established by case law (see, the paragraph bridging pages 10 and 11 of the Office Action). However, the Examiner failed to indicate the evidence that shows that using high frequencies as claimed in the instant claims 116 and 164 is just "optimization" or that it was achieved by "routine experimentation." Even if the Examiner were correct, under the authority of *In re Browner*, a positive suggestion of the desirability of modification is needed, as

discussed in the response to the previous Office Action. Such suggestion is clearly absent.

It appears to the Applicant that the Examiner is relying on the "obvious-to-try" approach by stating that in this case it is "obvious to vary and/or optimize." It is, however, a well settled law that "obvious-to-try" approach cannot be used when "trying" means varying a parameter until a successful result has been achieved, where the reference does not indicated which variation were likely to be successful.

Furthermore, previously, the Applicant explained that Siegel et al. teach that as the frequency is progressively increased from 25 to 243 KHz, the results on clot dissolution get progressively worse, and the degree of dissolution progressively falls from 99 %, to 86, 45, 44, 36, 27, and 26 %) (see, col. 7, lines 55-57). Thus, not only does Siegel et al. not provide any indication that moving towards higher frequencies may bring about any improvement, they clearly teach precisely to the contrary. Indeed, Siegel et al. emphasize the importance of the fact that "when ultrasound is applied at a lower, rather than a higher frequency, the effectiveness of the method is markedly enhanced" (col. 5, lines 29-31).

Therefore, the evidence unquestionably indicates that Siegel et al. explicitly teach that the results get worse when the frequency is increased from 25 KHz to 243, as described above. It is the Applicant's position that the results provided by Siegel et al. discourage those skilled in the art from moving towards even higher frequencies, thus teaching away from using any high frequencies. No person having ordinary skill in the art who studied the teachings of Siegel et al. would ever try to increase the frequency because Siegel et al. teach that the results will get worse than before. To follow such a path would be clearly unreasonable.

Therefore, it is submitted that one skilled in the art would not be motivated to modify the teachings of Siegel et al. towards the increase in frequency to 750 KHz or higher, because the teachings of Siegel et al. suggest that such modification will lead to worse results.

In addition, Porter cannot be used as a valid 35 U.S.C. § 103 reference, as discussed below. Therefore, the disclosure of Porter indicating a possibility of using frequencies in the range claimed in claims 116 and 164 cannot be used to modify Siegel et al. in a way suggested by the Examiner.

Indeed, it is well established that to qualify as a valid 35 U.S.C. § 103 reference, the reference must first qualify as prior art under a section of 35 U.S.C. § 102. See, Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir. 1987). The present application has the effective filing date June 19, 1996, i.e., the filing date of the parent application USSN 08/666,129 to which the present application claims priority. Accordingly, Porter having the publication date July 15, 1997 does not qualify as a 35 U.S.C. § 102(b) reference, but can potentially qualify only as a 35 U.S.C. § 102(e) reference, based on Porter's actual filing date of October 17, 1995.

The Applicant has executed a Declaration under 37 C.F.R. §1.131. As stated in the Declaration, this invention was conceived of and reduced to practice prior to the filing date of Porter. Therefore, the present invention was conceived of and reduced to practice prior to the earliest priority date Porter. Accordingly, in accordance with MPEP §§ 706.02(b) and 715.01, Porter is considered antedated for the purposes of 35 U.S.C. § 102 (e), and is not available for the purposes of making out a valid *prima facie* case of obviousness under 35 U.S.C. § 103.

In view of the foregoing it is submitted that each of claims 116 and 164 is patentably distinguishable over Siegel et al. in view of Porter. Each of claims 117-125,

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129-131, 138-141, 146-151, 160, 165, 166, 168-174, 178, and 179 depends, directly or indirectly either on claim 116 or on claim 164 and is considered patentable for at least the same reason. Therefore, reconsideration and withdrawal of the rejection of claims 116-125, 129-131, 138-141, 146-151, 160, 164-166, 168-174, 178, and 179 are respectfully requested.

In addition, claims 126-128 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Siegel et al., in view of Unger '381, and further in view of Porter, and further in view of U.S. Patent No. 5,542,935 to Unger et al. ("Unger '935")(page 17 of the Office Action). This rejection is respectfully traversed.

The Examiner has correctly indicated (page 17, fourth paragraph of the Office Action) that the combination of Siegel et al., Unger '381, and Porter fails to teach every limitation of claims 126-128, to wit, to teaching that the liposome can comprise certain phospholipids, such as dipalmitoylphosphatidylethanolamine or dipalmitoylphosphatidic acid. To eliminate this deficiency, the Examiner proposes to combine Siegel et al., Unger '381, and Porter with Unger '935.

However, Unger '935 is not available as a valid prior art reference for the purposes of a rejection under 35 U.S.C. § 103(a) for the following reasons. The subject matter of Unger '935 and the subject matter of the invention claimed in the present application were commonly owned, at the time the claimed invention was made, by Imarx Pharmaceutical Corp.

The commonality of ownership at the time the present invention was made can be seen from the fact that both Unger '935 and the present application were assigned by the respective inventors to Imarx Pharmaceutical Corp. The assignment of Unger '935 was made on July 10, 1995 (Reel 0075, Frame 0038), and the assignment of the parent application of the present application (now U.S. Patent No. 6,033,645) was made on July

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22, 1996 (Reel 010065, Frame 0021). The present application was assigned to Imarx LLC, a successor organization to Imarx Pharmaceutical Corp., on October 7, 1999 (Reel 011425, Frame 0046).

Unger '935 can only potentially qualify as a prior art reference under 35 U.S.C. § 102 (e) but does not qualify as a 35 U.S.C. § 102 (b) reference, because its publication date of August 6, 1996 is not one year before the effective filing date of the present application, which is June 19, 1996, as discussed above. Accordingly, under 35 U.S.C. § 103(c), Unger '935 may not be used as a reference against the present application for purposes of a rejection under §103(a), as per MPEP § 706.02(l).

In addition, the Porter reference, is also antedated, as described above, in view of the above-discussed Declaration of the inventor under 37 C.F.R. §1.131. Accordingly, Porter is not available as a reference for the purposes of the §103(a) rejection of claims 126-128.

Since the combination of art used by the Examiner to formulate the obviousness rejection requires using Unger '935, as well as using Porter, it is submitted that the §103(a) rejection is improperly taken and should be withdrawn. Reconsideration and withdrawal of the rejection of claims 126-128 are respectfully requested.

E. Double Patenting Rejection

Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, 178, and 179 stand rejected under the non-statutory, judicially created doctrine of obviousness-type double patenting over claims 1-77 of U.S. Patent No. 6,576,220.

Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, 178, and 179 also stand rejected under the non-statutory, judicially created doctrine of obviousness-type double patenting over claims 1-25 of U.S. Patent No. 6,716,412.

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Finally, claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, 178, and 179 also stand provisionally rejected under the non-statutory, judicially created doctrine of obviousness-type double patenting over claims 1-42 of U.S. Patent Application published as US 2004/0265393.

While the Applicants respectfully traverse this rejection, it is believed that this issue has become moot in view of the terminal disclaimer which accompanies this response. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

F. New Claims

By the present amendment, new claims 251-267 are proposed for entry. No new matter is recited in the new claims. Claim 251 includes all the limitations of currently pending claim 126. Since claim 126 is believed to be allowable, as discussed above, claim 251 is also believed allowable for the same reasons. Each of claims 252-267 depends on claim 251, and is believed allowable at least by the virtue of such dependency.

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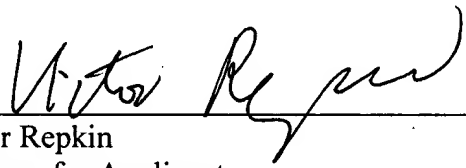
CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Check number 584822 in the amount of \$65.00 is enclosed as payment for the Terminal Disclaimer filing fee. No additional fee is believed due in connection with the filing of this paper. However, if any fee is due, the Commissioner is hereby authorized to charge any additional amounts required by this filing, or credit any overpayment, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal sheet is enclosed.

Respectfully submitted,

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